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AF/1617

21965

IN THE U.S. PATENT AND TRADEMARK OFFICE

Inventor	Gabor BOGYE
Patent App.	09/890,029
Filed	24 July 2001 Conf. No. 6045
For	PHARMACEUTICAL COMBINATION OF PROGESTERONE AND FOLIC ACID
Art Unit	1617 Examiner Hui, S

Hon. Commissioner of Patents
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Alexandria, VA 22313-1450

Appealed 27 May 2005

APPEAL BRIEF UNDER 37 CFR 41.37

Now comes appellant by his duly authorized attorney and submits his brief under the provisions of 37 CFR 41.37.

(i) REAL PARTY IN INTEREST

The real party in interest is the Appellant Gabor Bogye.

(ii) RELATED APPEALS AND INTERFERENCES

There are no prior or pending appeals, interferences or judicial proceedings known to Appellant or to the Appellant's legal representative, which may be related to, directly affect, or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(iii) STATUS OF CLAIMS

Claims 1 through 8, 14, 17 and 18 have been canceled.

Claims 9 through 13, 15, 16 and 19 through 25 have been rejected.

(iv) STATUS OF AMENDMENTS

Appellant filed an Amendment Under 37 CFR 1.116 After Final Rejection on 13 April 2005 in which no changes were made in the claims, but in which Appellant re-argued for the patentability of all pending claims over the prior art of record. In addition Appellant made of record a second search carried out by the European Patent Office in the corresponding European Patent Application. In the second European Search no references were cited that were not already of record in the present application and the search concluded that the claims in the European Patent Application were free of the prior art. Appellant had also made of record a complete version of the ALI et al reference, "Health Promotion and Osteoporosis Prevention Among Postmenopausal Women", Preventive Medicine, Vol. 24, 528 to 534 (1995). The Examiner's version of the ALI et al reference is merely an abstract. To the best of Appellant's knowledge the amendment after final rejection has been entered, but no claim has been allowed.

(v) Summary of Claimed Subject Matter

A first feature of the invention is a method of treating a patient undergoing treatment with a gestagen hormone composition

for hormone replacement therapy, for inflammation, for an in vitro fertilization program, for dermatological therapy or for cosmetological treatment to reduce a risk to the patient of thromboembolism induced by taking the gestagen hormone, which comprises the step of administering to the patient simultaneously, previously or subsequently to taking the gestagen hormone composition a therapeutically effective amount of a plasma homocysteine reducing agent. Antecedent basis for this aspect of the invention may be found in the specification on page 3, line 28 through page 6, line 32.

A second feature of the invention is a method of reducing a risk of thromboembolism induced by a gestagen hormone upon administration of said hormone to a patient for hormone replacement therapy, relieving inflammation, an in vitro fertilization program, dermatological therapy or cosmetological treatment comprising the step of administering to the patient simultaneously, previously or subsequently to taking the gestagen hormone composition a therapeutically effective amount of a plasma homocysteine reducing agent. Antecedent basis for this aspect of the invention may be found in the specification on page 3, line 28 through page 6, line 32.

A third feature of the invention is a method of treating an otherwise healthy patient taking a gestagen hormone composition for contraception to reduce a risk to the patient of thromboembolism induced by taking the gestagen hormone, which comprises the step of administering to the patient simultaneously, previously or

subsequently to taking the gestagen hormone composition for contraception, a therapeutically effective amount of a plasma homocysteine reducing agent. Antecedent basis for this aspect of the invention may be found in the specification on page 3, line 28 through page 6, line 32, page 7, lines 4 and 19, and page 8, line 3.

A fourth feature of the invention is a method of reducing a risk to an otherwise healthy patient of thromboembolism induced by administration of a gestagen hormone composition to said patient for contraception comprising the step of administering to the patient simultaneously, previously or subsequently to taking the gestagen hormone composition a therapeutically effective amount of a plasma homocysteine reducing agent. Antecedent basis for this aspect of the invention may be found in the specification on page 3, line 28 through page 6, line 32, page 7, lines 4 and 19, and page 8, line 3.

A fifth feature of the invention is a method of treating a patient taking a composition comprising a gestagen hormone to reduce a risk of thromboembolism induced by taking the gestagen hormone, which comprises the step of administering to the patient simultaneously, previously or subsequently to taking the composition comprising the gestagen hormone, a therapeutically effective amount of Vitamin B_{12}, betaine, choline or acetyl cysteine. Antecedent basis for this aspect of the invention may be found in the specification on page 3, line 28 through page 6, line 32.

(vi) Grounds for Rejection to be Reviewed on Appeal

The Examiner has rejected claims 9, 13 through 15, 17 and 18 under 35 USC 112, first paragraph, as beyond the scope of the enabling disclosure. The Examiner argues that the specification is not clear as to what is meant by "plasma homocysteine content reducing agent." Furthermore the Examiner argues that the specification does not enable one "skilled in the art" to determine what compounds or agents would in fact possess the ability to reduce plasma homocysteine content without the need to conduct undue experimentation. The Examiner believes that Appellant should limit his claims to the specific plasma homocysteine content reducing agents disclosed in the specification and in present claim 10. It is noted that claims 19 and 20 also relate to a "plasma homocysteine content reducing agent" though the Examiner has not included these claims in the rejection of the claims under 35 USC 112, first paragraph.

The Examiner has finally rejected all of the claims on appeal as anticipated under 35 USC 102. Claims 9 through 13, 15, 16, 21 and 22 have been rejected as anticipated in view of ALI et al in combination with the USDA Nutrient Database, Release 12, 1998 (Monograph No. 01077. Claims 19, 20, 23, 24 and 25 have been rejected as anticipated under 35 USC 102 in view of either the SPELLACY et al or BUTTERWORTH et al references.

(vii) The Arguments

35 USC 112, First Paragraph

The Examiner argues that the specification is not clear as to what is meant by "plasma homocysteine content reducing agent in violation of the description requirement of 35 USC 112, first paragraph." Furthermore the Examiner argues that the specification does not enable one "skilled in the art" how to determine what compounds or agents would in fact possess the ability to reduce plasma homocysteine content without the need to conduct undue experimentation as required by the enablement clause of 35 USC 112, first paragraph. The Examiner believes that Appellant should limit his claims to the specific plasma homocysteine content reducing agents disclosed in the specification and in present claim 10.

Appellant did not coin the terms "elevated plasma homocysteine concentration" or "plasma homocysteine content reducing agent." These terms and their meaning were well known to those skilled in the art at the time that the present application was constructively reduced to practice by the filing of the Hungarian priority application on 1 February 1999. See Welch, G.N., Loscalzo, J., Homocysteine and Atherothrombosis, New Eng. J. Of Med. 1998, 338, 1042 to 1050 cited on page 3 of the present application and made of record on PTO-1449 as reference (AO) and considered by the Examiner on 24 June 2004. The term "elevated plasma homocysteine concentration" is defined as homocysteine plasma concentration of at least 15μmol/liter, preferably at least 30μmol/liter and more

preferably at least 100μmol/liter. See page 1042, right-hand column of the reference. On page 1046 of the reference a number of specific compounds effective in reducing homocysteine plasma concentrations are indicated.

Appellant has made of record in his amendment of 24 September 2004 several publications to establish that one "skilled in the art" will be able to determine if any particular compound is an effective agent to reduce plasma homocysteine levels in patients with hyperhomocysteinemia without the need to carry out undue experimentation. In the Abbott Diagnostics Division, European Evaluations IMX, Homocysteine which was published in 1999, a collection of publications was included to show the use of the fully automated ABBOTT IMX Homocysteine Assay for the determination of plasma homocysteine level. The assay is fluorescence polarization immunoassay that is done with a kit. The assay is quick, inexpensive, and widely used both for animal tests and for humans at the patient's bedside.

The ABBOTT reference confirms that the determination of the plasma homocysteine level of a patient who may have hyperhomocysteinemia is a routine analysis that may be practiced by those skilled in the art without the need to carry out undue experimentation. It is also routine for one "skilled in the art" to use the ABBOTT IMX Homocysteine Assay to determine whether a compound possesses homocysteine plasma level reducing activity. In such a test the plasma homocysteine level is determined both before

and after administration of the test compound and the homocysteine plasma levels compared before and after said administration.

The ABBOTT IMX Homocysteine Assay is not the only way to determine the plasma homocysteine level of a patient who may have hyperhomocysteinemia and to determine whether a compound possesses homocysteine plasma level reducing activity. HPLC has been used for many years to achieve these ends. In the ABBOTT reference the ABBOTT assay is compared with assays based upon HPLC which has routinely been used for this purpose.

Appellant has made of record two references, namely, Clin Chem. 40/6, 873 to 881 (1994) and J. Of Chromatography, 422 (1987), pp 43 to 52 with his amendment of 24 September 2004 to further establish that HPLC has been used routinely for many years to determine the homocysteine plasma level in patients who may have hyperhomocysteinemia. Thus there is no reason why one "skilled in the art" having the present application before him would not be able to routinely determine if any particular compound has the ability to reduce homocysteine levels in plasma without the need to conduct undue experimentation.

Therefore Appellant should not be required to limit his claims to cover only the specific compounds disclosed in his application that have been established to reduce homocysteine plasma levels in patients. Not only has Appellant shown that the state of the art includes well-known assays to determine the plasma level of homocysteine, both before and after the administration of a compound that may be useful to this end, but furthermore there are

other specific compounds that are known in the art to have the ability to lower the plasma level of homocysteine. Penicillamine is a known reducer of plasma homocysteine levels. See Kang, SS, Wong, PW, Glickman, PB et al, Protein-Bound Homocysteine in Patients with Rheumatoid Arthritis undergoing D-Penicillamine Treatment, J. Clin. Pharmacol. 1986, 26:712 to 715 also made of record in Appellant's amendment of 24 September 2004.

There are also nucleoside analogs that are known to reduce plasma homocysteine levels. See Kredich, NM, Hershfield, MS, Falletta, JM, Kinney, TR, Mitchell, B and Koller, C, Effects of 2'-deoxycoformycin on homocysteine metabolism in acute lymphoblastic leukemia, Clin, Res. 1981, 29:541A.

The specification as filed should enable one "skilled in the art" to determine if any particular compound has the ability to reduce homocysteine plasma levels without the need to conduct undue experimentation. All claims now presented are based upon a specification that adequately describes the present invention and adequately enables one skilled in the art to practice the invention. Thus no rejection of any claim now presented should be maintained under 35 USC 112, first paragraph.

Furthermore the point of novelty in the present invention is not the plasma homocysteine reducing agents. Appellant does not contend that he has discovered any novel plasma homocysteine reducing agents. What Appellant has discovered is the administration of a plasma homocysteine reducing agent to a patient undergoing treatment with a gestagen hormone for the treatment of a

variety of illnesses to reduce a risk to the patient of thromboembolism. The risk of thromboembolism is reduced because the patient's plasma homocysteine level is lowered. No one else has ever administered to a patient undergoing therapy with a gestagen hormone, a compound for the stated purpose of reducing plasma homocysteine levels. The plasma homocysteine agent may be one of the specified vitamin co-factors disclosed on page 4 of the application or it may be penicillamine or a nucleoside analogue as disclosed in the prior art previously made of record by the Appellant in his amendment of 24 September 2004. It is also possible that in the future other researchers will find new plasma homocysteine reducing agents. Any potential new plasma homocysteine reducing agents may be tested according to the Abbott Laboratories protocol, made of record by Appellant in his amendment of 24 September 2004, and if successful should also fall within the scope of the presently claimed invention. The fact that Appellant has not himself discovered any new plasma homocysteine reducing agent does not mean that he must be limited only to those plasma homocysteine reducing agents known in the art.

It is perfectly proper to define an ingredient in functional terms, rather than in purely structural terms and such a definition of an ingredient is not beyond the scope of the enabling disclosure provided by the specification when the Appellant has given several representative examples in his application of compounds that are plasma homocysteine reducing agents, has provided collateral art to show additional compounds that are effective plasma homocysteine

reducing agents, and has provided a test to screen other compounds that are potential plasma homocysteine agents. The decisions cited by the Examiner do not relate to such a fact situation. One of the decisions, University of California v. Eli Lilly & Co., 43 USPQ 2d 1398 (CAFC 1997) relates to a biotechnology patent application where the ingredient defined in functional terms encompassed only novel nucleic acid molecules, none of which had actually been made, let alone tested. A more relevant decision is In re Angstadt and Griffin, 190 USPQ 214 (CCPA 1976) where the court held essentially that some experimentation is entirely permissible to still comply with the enablement clause of 35 USC 112, first paragraph, so long as the amount of experimentation required is not undue experimentation. In the present case, one "skilled in the art" could use the Abbott test described hereinabove to determine if any compound or composition is a plasma homocysteine content reducing agent as required by the claims without the need to conduct undue experimentation.

35 USC 102

The ALI et al Reference and the

Rejection of Claims 9 through 13, 15, 16, 21 and 22

The Examiner has rejected claims 9 through 13, 15, 16, 21 and 22 under 35 USC 102 as anticipated in view of ALI et al in combination with the USDA Nutrient Data Base, Release 12, 1998 (Monograph No. 01077. Claims 19, 20, 23, 24 and 25 have been rejected in view of either the SPELLACY et al or BUTTERWORTH et al

references. Appellant believes that no such rejection should be maintained against any claim on appeal. The ALI et al reference discloses the administration of a gestagen hormone to older female patients for the purpose of hormone replacement therapy. The ALI et al reference does not specifically disclose administering to the patients a plasma homocysteine reducing agent together with the gestagen hormone. However, ALI et al encourages the patient undergoing hormone replacement therapy to consume milk and milk products as well as other sources of calcium. The Examiner then has applied the USDA Nutrient Data Base, Release 12, 1998 (Monograph No. 01077) which discloses that milk contains a number of B Vitamins, including folic acid, Vitamin B_6 and Vitamin B_{12}. The Examiner concludes that such a patient described in ALI et al is inherently undergoing the same therapy as covered in the method of treatment of claims 9 and 15 and therefore ALI et al is anticipatory of these claims and the claims dependent upon these claims.

Appellant does not agree. It is clear in ALI et al that the patients undergoing hormone replacement therapy with a gestagen hormone are post-menopausal women at risk for osteoporosis. Accordingly ALI et al is concerned that the patients will have sufficient calcium intake so that osteoporosis can be minimized. Providing calcium intake is the sole reason mentioned in ALI et al for the patients to consume milk and milk products such as yogurt. Even though there is some B Vitamin content in milk, there is not the slightest suggestion in the ALI et al reference that the B

Vitamins are a factor at all in the treatment of those patients. Therefore there is no express disclosure or even a suggestion of the invention as covered in claims 9 and 15 and the claims dependent thereon in ALI et al.

Furthermore there is no inherent disclosure in ALI et al of the invention in claims 9 and 15. The USDA Nutrient Data Base, Release 12 indicates that a 100 g serving of milk (about 3.5 ounces of milk) contains 0.042 mg of Vitamin B_6, 5μg of folic acid, and 0.36 μg of Vitamin B_{12}. All three of these concentrations of B Vitamins are much lower than the therapeutically effective amount of the B Vitamins as defined in the specification on page 6, lines 25 to 30. Therefore there is no inherent disclosure in ALI et al of the present invention. In order to consume enough milk to obtain 0.5 mg of folic acid in a day (the minimum therapeutically effective daily dosage), the patient would have to consume 100 times the amount of milk shown in USDA Nutrient Data Base, Release 12, that is about 350 ounces of milk or about 10 liters of milk per day. For Vitamin B_6 in order to obtain the minimum therapeutically effective daily dosage of 10 mg, the patient would have to consume about 830 ounces of milk per day, well above 10 liters. For Vitamin B_{12} in order to obtain the minimum therapeutically effective daily dosage of 300μg, the patients would have to consume about 2900 ounces of milk per day which is almost 100 liters. These amounts of milk are not realistic figures in terms of a patient's diet and so it is not seen how ALI et al either anticipates under

35 USC 102 or renders obvious under 35 USC 103 the invention in claims 9 and 15.

The BUTTERWORTH et al and SPELLACY et al References and the Rejection of Claims 19, 20, 23 and 24

Appellant maintains that neither the BUTTERWORTH et al nor the SPELLACY et al reference inherently anticipates claims 19, 20, 23, or 24. Independent claims 19 and 20 define the patient as "an otherwise healthy patient taking a gestagen hormone composition for contraception to reduce the risk to the patient of thromboembolism induced by taking the gestagen hormone." SPELLACY et al discloses administration of 30 mg of Vitamin B_6 (see page 267, near the bottom) together with a gestagen hormone for female contraception to correct the adverse effects of the gestagen hormone on carbohydrate metabolism. This is a different utility from that of the presently claimed method of treatment where plasma homocysteine levels are lowered by catalytic metabolism of the homocysteine using Vitamin B_6 as a cofactor. The Examiner argues, however, that all patients undergoing gestagen therapy have elevated plasma homocysteine levels even though the prior art does not expressly say so when the SPELLACY et al patients undergo gestagen hormone therapy, they have elevated homocysteine levels, and when those same patients also take Vitamin B_6, those plasma homocysteine levels must drop.

Appellant emphasizes that the patient treated according to claims 19 and 20 is characterized as "an otherwise healthy patient"

which means that the patient does not suffer from the side effects of carbohydrate metabolism disruption. Thus the SPELLACY et al reference does not inherently anticipate independent claims 19 and 20 and the claims dependent thereon.

In BUTTERWORTH et al the situation is similar. Female patients receiving a gestagen hormone for contraception also take folic acid in a dosage of 10 mg/day. The patients are receiving the folic acid not for reducing an elevated plasma homocysteine level, but are receiving folic acid to treat dysplasia of the uterine cervix. This cytological effect sometimes results when women take gestagen hormones for contraception. In claims 19,20, 23 and 24, the patients are characterized as "otherwise healthy patients" meaning that these patients do not have dysplasia of the uterine cervix. Thus BUTTERWORTH et al does not inherently anticipate any of these claims.

Nor is there any suggestion in either SPELLACY et al or BUTTERWORTH et al to carry out the method of treatment on an otherwise healthy patient according to claims 19, 20, 23 or 24 and so there is no basis to reject these claims as obvious under 35 USC 103.

The BUTTERWORTH et al and SPELLACY et al References and the Rejection of Claim 25

Claim 25 defines the patient more broadly than do claims 19, 20, 23 and 24 in that the patients undergoing treatment with a gestagen hormone are not necessarily "otherwise healthy patients."

Nor are the patients limited to patients receiving contraception. However, in claim 25 the plasma homocysteine-reducing agent administered in conjunction with the gestagen hormone is limited to Vitamin B_{12} , betaine, choline or acetyl cysteine, none of which is either disclosed by or suggested by either SPELLACY et al or BUTTERWORTH. Accordingly there is no basis to reject claim 25 as either anticipated under 35 USC 102 or as obvious under 35 USC 103 in view of either SPELLACY et al or BUTTERWORTH et al.

Appellant now has the following direct comments regarding the patentability of all of the claims on appeal:

As for the publication ALI et al cited by the Examiner in the final rejection, the text of the full publication was not considered by the Examiner, as only the abstract was included with the office action. Appellant has obtained and has made of record with his second amendment of 13 April 2005, a copy of the full ALI et al publication. On page 532, col. 2, lines 1 through 3, the following is written:

Although hormone users reported higher calcium intake and greater exercise participation than non-users, the difference was not significant.

This sentence provides further evidence that women taking HRT did not take therapeutically effective amounts of plasma homocysteine content reducing agents occurring in milk (e.g. folic acid). The abstract includes only the first part of the above cited sentence and the important end of the sentence i.e. "the difference was not significant" is missing from the abstract.

Appellant specifically tested his contraceptive patients for carbohydrate metabolism problems and none of the patients had this problem. Thus all of Appellant's contraceptive patients were otherwise healthy. The SPELLACY et al reference discloses contraceptive patients who have developed carbohydrate metabolism disorders while undergoing the contraception. Thus the SPELLACY et al patients are different patients from the patients treated according to the presently claimed invention, including the patients receiving contraception. Appellant also emphasizes that the taking of gestagen hormones as contraceptives is contraindicated for patients having carbohydrate metabolism disorders.

The Examiner has alleged that all patients taking progesterone (a gestagen hormone) have elevated homocysteine levels in the blood because homocysteine-elevating activity of progesterone is inherently present in all patients taking this drug. The Examiner has not provided any documentary evidence to support this assertion. Appellant cannot confirm that all patients taking a gestagen hormone for contraception or for any other medicinal purpose have elevated plasma homocysteine levels. All of Appellant's patients were healthy patients; they has neither a carbohydrate metabolism disorder nor a Vitamin B_6 depletion disorder.

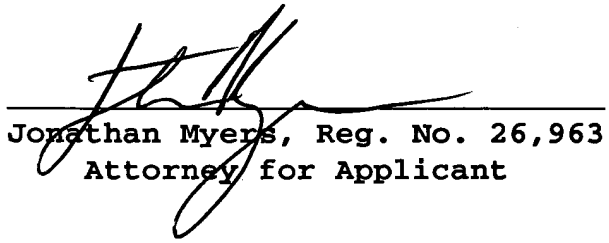
The Examiner notes that the prior art that he has cited is silent with regard to the patient's plasma homocysteine levels. According to the BRATTSTROM et al reference cited and discussed in

the background portion of the present application on page 3 and made of record on 2 January 2002 in an Information Disclosure Statement, not all patients taking a gestagen contraceptive have elevated plasma homocysteine levels though there is evidence that all of these patients do suffer from a depletion of the B Vitamin co-factors. No connection is disclosed in BRATTSTROM et al between gestagen hormone administration and elevated plasma levels of homocysteine. Accordingly the correlation between the administration of a gestagen hormone to patients and elevated plasma homocysteine levels in the patient was found by the Appellant and was not in the prior art. Thus there is no general recognition in the prior art that there is a direct correlation between administration of a gestagen hormone to a patient and an increase in the plasma concentration of homocysteine in that patient.

In view of the above it is believed that no claim on appeal should be rejected either as anticipated under 35 USC 102 or as obvious under 35 USC 103.

Appellant respectfully requests that the Board of Appeals and Interferences reverse the Examiner's rejection of all claims. Appellant has included payment for submission of this appeal brief through the credit card of the undersigned attorneys. Form 2038 is enclosed.

Respectfully submitted,
The Firm of Karl F. Ross P.C.



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Enclosure: PTO 2038

(viii) Claim Appendix

9. A method of treating a patient undergoing treatment with a gestagen hormone composition for hormone replacement therapy, for inflammation, for an in vitro fertilization program, for dermatological therapy or for cosmetological treatment to reduce a risk to the patient of thromboembolism induced by taking the gestagen hormone, which comprises the step of administering to the patient simultaneously, previously or subsequently to taking the gestagen hormone composition a therapeutically effective amount of a plasma homocysteine reducing agent.

10. The method of treatment defined in claim 9 wherein the plasma homocysteine reducing agent is a compound selected from the group consisting of folic acid, Vitamin B_6, Vitamin B_{12}, betaine, choline, and acetylcysteine.

11. The method of treatment defined in claim 9 wherein the plasma homocysteine reducing agent is folic acid.

12. The method of treatment defined in claim 9 wherein the plasma homocysteine reducing agent is Vitamin B_6.

13. The method of treatment defined in claim 9 wherein the gestagen hormone composition contains a progesterone.

15. A method of reducing a risk of thromboembolism induced by a gestagen hormone upon administration of said hormone to a patient for hormone replacement therapy, relieving inflammation, an in vitro fertilization program, dermatological therapy or cosmetological treatment comprising the step of administering to the patient simultaneously, previously or subsequently to taking the gestagen hormone composition a therapeutically effective amount of a plasma homocysteine reducing agent.

16. The method of reducing a risk of thromboembolism defined in claim 15 wherein the plasma homocysteine reducing agent is a compound selected from the group consisting of folic acid, Vitamin B_6, Vitamin B_{12}, betaine, choline, and acetylcysteine.

19. A method of treating an otherwise healthy patient taking a gestagen hormone composition for contraception to reduce a risk to the patient of thromboembolism induced by taking the gestagen hormone, which comprises the step of administering to the patient simultaneously, previously or subsequently to taking the gestagen hormone composition for contraception, a therapeutically effective amount of a plasma homocysteine reducing agent.

20. A method of reducing a risk to an otherwise healthy patient of thromboembolism induced by administration of a gestagen hormone composition to said patient for contraception comprising the step of administering to the patient simultaneously, previously or subsequently to taking the gestagen hormone composition a therapeutically effective amount of a plasma homocysteine reducing agent.

21. The method of treating a patient defined in claim 9 wherein the patient has an elevated plasma homocysteine level resulting from taking a gestagen hormone composition.

22. The method of reducing a risk of thromboembolism in a patient as defined in claim 15 wherein the patient has an elevated plasma homocysteine level resulting from taking a gestagen hormone composition.

23. The method of treating an otherwise healthy patient as defined in claim 19 wherein the patient has an elevated plasma homocysteine level resulting from taking a gestagen hormone composition.

24. The method of reducing a risk to an otherwise healthy patient of thromboembolism as defined in claim 20 wherein the patient has an elevated plasma homocysteine level resulting from taking a gestagen hormone composition.

25. A method of treating a patient taking a composition comprising a gestagen hormone to reduce a risk of thromboembolism induced by taking the gestagen hormone, which comprises the step of administering to the patient simultaneously, previously or subsequently to taking the composition comprising the gestagen

hormone, a therapeutically effective amount of Vitamin B_{12}, betaine, choline or acetyl cysteine.